REMARKS

1. Applicant thanks Examiner Venkat for her kind assistance, provided during a telephone interview on July 3, 2002. During the interview, Applicant expressed grave concern about the informal nature of the rejections made by Examiner Gitomer and the disparaging comments made with regard to the invention, for example at line 22 on page 2 of the Office Action. Applicant expressed the opinion that Examiner Gitomer's remarks are evidence of a bias that minimizes the possibility that the application will be fairly examined and requested that the application by reassigned to another Examiner. Examiner Venkat requested applicant to provide her advance notice of the filing of this response and assured Applicant that she would monitor prosecution of the application. In response to Applicant's expressed concern about the lack of factual or substantive basis in many of Examiner Gitomer's rejections, Examiner Venkat counseled Applicant to respond to the rejections to the best of its ability.

Applicant also thanks Examiner McKane for his assistance during a brief telephone conversation on the morning of August 20, 2002. Applicant reiterated its concerns and Examiner McKane recommended that Applicant interview Examiner Gitomer shortly after the current response is filed. He also agreed that Applicant's request that examination in the current case be closely monitored by a third party in a supervisory capacity was a fair and legitimate request, and that he was available for further consultation if necessary.

2. Applicant has amended Figures 1 – 4 to provide a unit of time for the horizontal axes. Support for the amendment is found in the specification at page 6, line 28 to page 7, line 4. A calibration visit is described as being eight hours in length, lasting, as shown in Figure 1, for example, from approximately .33 to approximately .67. Thus, one skilled in the art would understand that the

horizontal axis of Figure 1 is expressed as a portion of a 24-hour day. Accordingly, the horizontal axes of Figure 1 – 4 bear the legend: "Time (Part of a day)."

3. The specification has been amended as in several places to correct typographical and spelling errors.

4. Table 1 has been amended by deleting the columns "DOB" and "Ethnicity." The columns were omitted because the data contained was not essential to an understanding of the invention, and the omission of the two columns corrected observed formatting problems. Table 2 has been amended to correct a math error in col. 5, row 4.

5. Page 10, line 3 to line 10 has been amended to substitute the term "glucose concentration" for "glucose level," equivalent terms both referring to the amount of glucose contained in a unit volume of a subject's blood. Additionally, as amended the glucose concentrations are expressed as mg/dL to harmonize this paragraph with the remainder of the application, for example page 8, line 19 to line 31. Concentration is alternately expressed as mM. One skilled in the chemical arts will readily recognize that the units are equivalent.

6. To improve readability, page 10, line 13 to line 19 has been amended to indicate that the maximum and minimum values are 300 mg/dL and 90 mg/dL, respectively, as previously indicated at page 8, line 21 to line 22.

7. New Claim 35 has been added to the application. Support for the amendment is found in the specification at page 5, line 30 to page 8, line 9. In view of the addition of Claim 35, Claims 1 – 13 have been amended to correct their dependencies.

8. Applicant avers that no new matter was added by way of the above amendments.

9. The Abstract is objected to. The Abstract has been cancelled from the application and a new one substituted that complies with all formal requirements.

10. The Examiner characterizes the Claims as being "essentially meaningless and totally obvious at the same time" at page 2, line 22 to line 23 of the Office Action. Applicant vigorously objects to such language. The characterization is not made within the context of a proper rejection under 35 USC §'s 112 or 103, and therefore has nothing to do with the merits of the Claims. The remark is thus little more than a casual statement of a personal nature that disparages the invention. The Examiner is respectfully reminded that such comments are not properly made part of the Official Record. MPEP § 707.07(d). Accordingly, Applicant respectfully requests that the offending material be expunged from the Official Record.

11. Claims 1 – 34 stand rejected under 35 USC § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. In part, the rejection is based on a number of informalities, such as lack of antecedent and typographical errors. Applicant has amended the Claims to correct such informalities.

Regarding Claims 1, 14 and 24: The Examiner finds the formula of Claim 1 to be meaningless because no units are presented. Responsive thereto, Applicant has amended to Claim 1 to specify that TARGET and STARTING refer to blood glucose concentration. Thus, one skilled in the art would understand that the units must be either mg/dL or mM. The Examiner is respectfully reminded that the X value constitutes an index, and thus doesn't need to be expressed in units. Claim 1 is further amended to specify that the index is derived based on

the type of diabetes and the degree of control over the condition, as described in the specification at page 13, line 22 to line 25. Claims 14 and 24 have been similarly amended. Claim 1 has been further amended to depend from new Claim 35, describing a method of generating a glycemic profile in a subject having a predetermined shape, wherein the steps of Claim 1 are recast as sub-steps within the method of Claim 35.

Regarding Claims 4 and 5: In view of the amendments to Claim 1, the rejection of Claims 4 and 5 is deemed overcome. Furthermore, in Claim 5, the index is described in greater detail.

Regarding Claim 8: The informality in Claim 8 has been corrected.

Regarding Claims 12 and 23: Applicant respectfully disagrees that Claim 12 is meaningless. The Examiner's finding appears to be based on an understanding that the Claim itself needs to provide an enabling description of the invention. The subject matter of page 5, line 30 to page 8, line 9 would enable one having an ordinary level of skill in the art of developing calibrations for spectroscopic applications to practice the invention. As such, the rejection of Claim 12 under 35 USC § 112, second paragraph is deemed to be improper. Similarly, the rejection of Claim 23 is deemed to be improper.

Claims 2, 6, 7, 13,15,18, 19, 25, 27, 29, 30 and 34 have been cancelled from the application. Accordingly, the rejections of the Claims are rendered moot.

Regarding Claims 3, 9, 10, 11, 16, 17, 20, 21, 22, 26, 28, and 31 – 33: The addition of independent Claim 35, and amendments to the independent Claims have overcome all remaining rejections under 35 USC § 112, second paragraph. In many cases, use of alternate terminology in the Claims from which they depend has necessitated amendments to these dependent Claims.

11. The Examiner stated that the Claims could not be properly searched. However, Applicant notes that the International Search Authority performed a search of the same Claims in the corresponding PCT application without difficulty.

CONCLUSION

While the Applicant has made every effort to address each and every one of the Examiner's concerns, the unusual form of the rejections in many cases has rendered clear-cut responses difficult to formulate. Nevertheless, Applicant considers itself to have fully complied with Examiner Venkat's direction to respond to the rejections to the best of its ability. Therefore, Applicant deems itself to have fully satisfied the requirements of 37 CFR § 1.111. Furthermore, the Claims are deemed to be in allowable condition. As such, the Examiner is earnestly requested to withdraw all objections and allow the Application to pass to issue as a U.S. Patent. Should the Examiner have any questions regarding the Application, he is urged to contact Applicant's attorney at the telephone number given below.

Respectfully submitted.

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AMENDMENT (MARKED-UP COPY)

In the title:

Please amend the title of the Application to:

A Method of Producing a Glycemic Profile of Predetermined Shape in a Test Subject.

In the Figures:

Figures 1 – 4 have been amended to provide a unit of time for the horizontal axis. Redlines showing the amendment have been provided herewith.

In the specification:

Page 1, line 20 to page 2, line 7:

The increase in blood sugar levels resulting from the ingestion of carbohydrate foods has long been known; in fact it is of ongoing concern in those afflicted with diabetes mellitus. Furthermore, carbohydrate intolerance is one of the major criteria for a diagnosis of diabetes mellitus. The Oral Glucose Tolerance test employs ingested carbohydrate in a predetermined form and amount to quantify a test subject's response to a resulting glucose challenge. See *Oral glucose tolerance test,* Complete Guide to Medical Tests, http://www.healthgate.com/tests/tests/test240.shtml. Criteria have been established to evaluate this response according to the type of diabetes to be diagnosed. In the case of gestational diabetes, a blood glucose level exceeding 180 mg/d[l]L is indicative of an impaired insulin response and therefore suggestive of diabetes. See *Oral glucose tolerance test for gestational diabetes*,

http://www.medstudents.com/ginob/ginob4t1.htm. In the case of Type 1 or Type 2 diabetes, a blood glucose level exceeding 200 mg/d[l]L is indicative of an impaired insulin response. While the blood glucose excursion may fall back to normal over a period of time, the [O]oral glucose tolerance test is concerned only with the peak blood level of glucose. It does not concern itself with the rate of change in glucose levels or the amount of time it takes for glucose levels to fluctuate from a high point to a low point.

Page 8, line 19 to page line 31:

In order to provide a broad range of reference glucose values, a target glucose profile for each calibration visit was specified as a glucose level range of from less than 90 mg/dL through a targeted high of greater than 300mg/dL for each calibration visit, with a rate of change < 5 mg/d[l]L/minute. As previously explained, it was necessary to obtain data sets in which the patterns resulting from the blood glucose reference values did not correlate across calibration visits; in other words, they were to be very dissimilar to each other. Therefore, the glycemic profiles were to be anti-correlated pairs; that is, one profile of a pair was to be the inverse of the other profile of the pair. During a first calibration visit, a glucose excursion that mimicked the first profile of a pair was to be achieved. The goal for a second visit was to achieve a glucose excursion that mimicked the second profile of the pair. Both calibration visits were eight hours in duration.

Page 9 – 10, Table 1:

	Sex	*[DOB*	*Ethnicity]*	*Diabetes Status*	*Year of Diagnosis*	*Health Status*	*Proteinuria*	*A1C*
1	F	[6/10/58	HIS]	2	1991	Good	1+	7.4
2	M	[11/08/6	CAU]	2	1994	Good	Neg	6.9
3	M	[01/23/4	CAU]	2	1993	Good	Neg	6.0

4	F	[06/26/0	CAU]	1	1982	Good	Neg	6.0
5	M	[08/23/3	CAU]	2	1998	Fair	Neg	6.1
6	M	[05/07/6	CAU]	2	1999	Good	1+	6.5
7	M	[01/18/7	CAU]	2	1996	Good	2+	5.5
8	F	[02/24/4	CAU]	1	1964	Good	Trace	7.5
9	F	[04/02/5	HIS]	2	1994	Good	Trace	7.5
10	F	[05/22/3	CAU]	2	1998	Good	Neg	5.3

Page 10, line 3 to line 10:

The formula used to calculate the amount of carbohydrate required to produce the desired glucose excursion is:

$$CHO = \frac{TARGET - STARTING}{X}, \qquad (1)$$

where *CHO* is the amount of carbohydrate in grams, 'Target' is the glucose [level] concentration to be achieved, typically expressed either as mg/dL or mM, 'Starting' is the current glucose [level] concentration, also expressed as mg/dL or mM, and *X* is a numerical index of the subject's sensitivity to carbohydrate challenge, described in greater detail below.

Page 10, line 12 to line 19:

Table 2, below, shows a maximum and minimum, range and standard deviation of the glucose values for calibration visits of all clients. Maximum is the highest value achieved during a glucose excursion; minimum is a low value that may precede or follow a maximum value and the range is the span between maximum and minimum. As the results show, the target maximum (300mg/dL)

and minimum values (90mg/dL) were achieved in ten out of twenty-three visits. Three subjects out of ten achieved the target range for both visits one and two.

Page 10 to page 11, Table 2:

		Entire Day			
Subject	Visit	Max	Min	Range	STD
1	1	287	103	184	68.0
1	2	228	57	171	48.0
2	1	313	66	247	87.0
2	2	379	76	303	97.1
3	1	326	62	264	90.9
3	2	297	71	226	68.2
4	1	399	40	359	103.7
4	2	372	64	308	95.1
5	1	283	70	213	49.1
5	2	326	75	251	88.1
6	1	234	97	137	42.7
6	2	345	102	243	82.9
7	1	331	44	287	99.3
7	2	230	58	172	49.8
7	3	287	97	190	60.2
8	1	395	74	321	98.3
8	2	357	74	283	88.2
8	3	390	54	336	99.0
9	1	255	103	152	36.3
9	2	217	75	142	56.7
9	3	196	70	126	40.0
10	1	173	67	106	36.8
10	2	207	85	122	36.7

Page 11, line 23 to page 12, line 9:

The rate of change between the maximum glucose level and minimum glucose level was calculated for the first calibration visit (Table 2). This was calculated according to:

$$Rate\ of\ change = \frac{(max\ glucose)-(min\ glucose)}{(max\ time)-(min\ time)}. \qquad (2)$$

The rate of change is expressed as milligrams per deciliter (mg/d[l]L) over minutes. The rate of change is an indicator of a subject's capacity for the movement in blood glucose necessary to achieve the targeted glucose profile. The targeted glucose profile's rate of change is ±1.33(mg/[(]d[l)]L/minute. For calibration visit one, the rate is a negative value, since it describes a downward trend. As Table 3, below, shows, three subjects (4, 5, and 6) had rates similar to that of the targeted profile.

Page 13, line 22 to line 11:

'*X*' is a factor that serves as an index to carbohydrate sensitivity. The initial value is assigned by the clinician, according to type of diabetes and level of diabetes control, from a range of approximately 1 to 3, and is subsequently individualized to the subject. The amount of carbohydrate required to produce a target glucose excursion is calculated using a starting, generalized value of X, assigned by the clinician, as previously described. The diabetic subject then ingests the calculated amount of carbohydrate. Blood glucose values are measured at regular intervals until the subject's blood glucose values reach a maximum. The actual maximum and the target maximum are compared and an individualized value of X, X_i is calculated according to:

$$X_i = \frac{OBSERVED - STARTING}{CHO}, \qquad (4)$$

where *'OBSERVED'* represents the observed maximum, as contrasted with the target maximum. Thus, for an individual, assigned an initial *X* value of 2, who attained a maximum of 297mg/dL following ingestion of an amount of carbohydrate calculated to produce a maximum of 350mg/d[l]L, the individualized value of *X*, X_i, would be calculated as 1.7. This calculated value can be used by the subjects to further enhance their diabetes management. It can be assessed that the Type I clients (4 and 8) had a much higher sensitivity to carbohydrates (2.10 and 3.09, respectively) than the other clients. Table 4

below provides the sensitivity factors and Carbohydrate quantities employed for visit one profiles.

Page 14, line 16 to line 25:

The calibration visits also provide an educational experience for the diabetic subjects. The test subjects indicate a greater awareness of the impact of carbohydrate foods on their blood glucose levels. Subjects who experience higher sensitivities in the morning may choose to move more of their carbohydrate food choices to the afternoon or evening, when their medication regimen may produce lower sensitivities. Furthermore, subjects report that their intake of carbohydrate is generally reduced, that they typically take smaller-sized portions of carbohydrate foods, and that nutritional information from food labels is more meaningful, all highly desirable outcomes in the management of diabet[e]*ic* conditions.

In the abstract:

Please cancel the abstract from the Application and insert the following new Abstract:

A method of generating a glycemic profile in a subject having a predetermined shape employs a formula for calculating the amount of carbohydrate necessary to achieve a target maximum in a subject's blood glucose concentration based on a baseline blood glucose level, target maximum and an index of subject's sensitivity to carbohydrate. Initially, the index value is an exemplary value based on typical carbohydrate sensitivities displayed by various types of diabetics. However, the index may be individualized to a test subject based on an actual glucose excursion. Blood glucose is driven to a target minimum through administration of a hypoglycemic agent, and rate of change is substantially conformed to a target rate, so that resulting profile is uncorrelated to factors other than blood glucose concentration. Furthermore, a method for dietary management of a diabetic's glycemic profile, wherein an optimal glycemic profile is achieved and maintained, also incorporates the formula.

In the Claims:

1. (Amended) A method [for shifting blood glucose level in an individual from a starting value to a target value] as in Claim 35, [said method] further comprising the step[s] of:

calculating [a] said required amount of carbohydrate [to ingest to produce said shift] according to a formula, said formula comprising:

$$CHO = \frac{TARGET - STARTING}{X},$$

where *CHO* represents said required amount of carbohydrate, *TARGET* represents said target maximum, *STARTING* represents a starting blood glucose concentration, and *X* comprises an index representing said subject's sensitivity to carbohydrate[;], said index based on said subject's diabetic status and ease with which said status is controlled.

[ingesting said first required amount of carbohydrate by said individual; and

observing an actual shift in blood glucose value caused by ingesting said required amount of carbohydrate.]

3. (Amended) The method of Claim [2] 35, wherein said carbohydrate [is] includes any of:

conventional liquid food;

conventional solid food; and

conventional liquid and solid food.

4. (Amended) The method of Claim [2] 1, wherein *X* comprises a generalized value.

5. (Amended) The method of Claim 4, wherein [said generalized value] $\underline{X}$ is from [the] a range of approximately 1 to 3, wherein 1 represents low carbohydrate sensitivity and wherein 3 represents high carbohydrate sensitivity.

8. (Amended) The method of Claim [7]1, further comprising the step of:

individualizing [said value of] X to said [individual] subject based on an actual elevation of blood glucose [excursion] concentration resulting [when said individual ingests] from ingesting said calculated amount of carbohydrate according to:

$$X_i = \frac{OBSERVED - STARTING}{CHO},$$

where ['Observed'] *OBSERVED* represents an observed blood glucose [value] concentration following [said] ingestion of said [first] calculated amount of carbohydrate, and wherein X_i represents [said] an individualized value of X.

9. (Amended) The method of Claim 8, further comprising the step of:

calculating a second required amount of carbohydrate using [said individualized value of X] $\underline{X_i}$, wherein said second [required] amount comprises [the] amount [of carbohydrate] required [to be ingested] by said [individual] subject to [effect] achieve elevation of said subject's blood glucose concentration to said target [glucose excursion] maximum.

10. (Amended) The method of Claim 9, further comprising the step of:

ingesting said second required amount of carbohydrate by said [individual] subject.

11. (Amended) The method of Claim 9, further comprising the step of:

achieving and maintaining an optimal glycemic profile based on said formula and [said individualized value of X] $\underline{X_i}$.

12. (Amended) The method of Claim 10, further comprising the step of:

generating an individualized calibration model for said [individual] subject for use in non-invasive methods of blood glucose determination employing spectroscopic instrumentation based on idealized ant-correlated glycemic profiles produced using said formula.

14. (Amended) A method of dietary management of a[n individual's] subject's glycemic profile, wherein an optimal glycemic profile is achieved and maintained, said method comprising the steps of:

calculating an amount of carbohydrate required to [ingest to shift blood glucose level in said individual] induce an elevation in said subject's blood glucose concentration to a target maximum according to a formula, said formula comprising:

$$CHO = \frac{TARGET - STARTING}{X},$$

where ['Target represents said target value, 'Starting' represents said first value, and] CHO represents said required amount of carbohydrate, $TARGET$ represents said target maximum, $STARTING$ represents a starting blood glucose concentration, and [wherein] X [represents] comprises a generalized index value representing said subject's sensitivity to carbohydrate, said index based on said subject's diabetic status and ease with which said status is controlled;

ingesting said required amount of carbohydrate by said [individual] subject;

[observing] measuring actual [shift] elevation in blood glucose [value] concentration caused by ingesting said required amount of carbohydrate;

generating a value of X individualized to said [individual] subject, X_i; and

achieving and maintaining an optimal glycemic profile based on said formula and [said individualized value of X] X_i.

16. (Amended) The method of Claim 13, wherein said carbohydrate [to ingest is] includes any of:

conventional liquid food;

conventional solid food; and

conventional liquid and solid food combined.

17. (Amended) The method of Claim 14, wherein [said generalized value of] X is from a range of approximately 1 to 3, wherein 1 represents low carbohydrate sensitivity and wherein 3 represents high carbohydrate sensitivity.

20. (Amended) The method of Claim [19] 14, wherein said generating step comprises:

individualizing X to said [individual] subject based on an actual elevation of blood glucose [excursion] concentration resulting from ingesting said [first] calculated amount of carbohydrate[,] according to:

$$X_i = \frac{OBSERVED - STARTING}{CHO},$$

where ['Observed] *OBSERVED* represents an actual blood glucose [value] concentration achieved [following said ingestion of] when said subject ingests said [first] calculated amount of carbohydrate [wherein] and X_i represents said individualized value of X.

21. (Amended) The method of Claim 20, wherein [said] achieving and maintaining [step] an optimal glycemic profile comprises the steps of:

calculating a second required amount of carbohydrate to ingest to achieve and a maintain said optimal glucose profile based on said formula and [said individualized value of X] X_i; and

ingesting said second required amount in divided portions over a predetermined time span.

24. (Amended) A method of predicting a required amount of carbohydrate to ingest to [shift] produce an elevation in blood glucose [level] concentration in a[n individual] subject from a starting value to a target [value] maximum, said method comprising the steps of:

providing said target[value] and [said] starting value[s]; and

[calculating a difference between said values; and]

calculating said required amount of carbohydrate [by dividing said difference by a numerical index representative of said individual's sensitivity to carbohydrate] according to a formula, said formula comprising:

$$CHO = \frac{TARGET - STARTING}{X},$$

where[in] *CHO* represents said required amount of carbohydrate, *TARGET* represents said target maximum, *STARTING* represents a starting blood glucose concentration, and X [represents said numerical index] comprises a generalized index representing said subject's sensitivity to carbohydrate, said index based on said subject's diabetic status and ease with which said status is controlled.

28. (Amended) The method of Claim 24, wherein [said generalized value] X is from [the] a range of approximately 1 to 3, wherein 1 represents low carbohydrate sensitivity and wherein 3 represents high carbohydrate sensitivity.

31. (Amended) The method of Claim [30] 24, [wherein said value of X is individualized based on an actual glucose excursion resulting when said individual ingests said first calculated amount of carbohydrate according to] further comprising the step of:

individualizing X to said subject based on an actual elevation of blood glucose concentration resulting from ingesting said calculated amount of carbohydrate according to:

$$X_i = \frac{OBSERVED - STARTING}{CHO},$$

wherein ['Observed'] *OBSERVED* represents an actual blood glucose [value] concentration achieved following [said] ingestion of said required amount of carbohydrate, and X_i represents said individualized value of X.

32. (Amended) The method of Claim [31] 24, further comprising the step of:

achieving and maintaining an optimal glycemic profile [based on said formula and said individualized value of X].

33. (Amended) The method of Claim [31] 24, further comprising the step of producing idealized, anti-correlated glycemic profiles in a[n individual] subject [based on said formula and said invidualized of X] so that individualized calibration models may be generated for use in non-invasive methods of blood glucose determination employing spectroscopic instrumentation.

Please insert new Claim 35 as follows:

35. A method of generating a glycemic profile in a subject having a predetermined shape, comprising the steps of:

driving said subject's blood glucose concentration to a target maximum through oral ingestion by said subject of a calculated amount of carbohydrate required to achieve said target maximum;

monitoring said individual's blood glucose concentration at predetermined time intervals; and

driving said subject's blood glucose to a target minimum through administration of a hypoglycemic agent;

wherein rate of change of said glucose concentration substantially corresponds to a target rate; and

wherein a resulting glycemic profile is minimally correlated to factors other than subject's blood glucose concentration.

Please cancel Claims 2, 6, 7, 13, 15, 18, 19 25, 27, 29, 30 and 34 from the Application.